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THE ELIMINATION OF CHLORIDES IN FEVER

[Following is a translation of a prize essay by F. Röhmann in the German-language periodical <u>Zeitschrift für Klinische Medicin</u> (Journal of Clinical Medicine), Vol 1, 1880, pages 513-535.]

<u>Introduction</u>

By a prize contest announced [see note] by the Medical Faculty in Berlin I was motivated to conduct in the laboratory of Privy Councilor Prof. Dr. Leyden's propaedeutic clinic a series of investigations of the elimination of chlorine in fever, the results of which I report below.

[Note] The subject was announced as follows: "The elimination of chlorides in febrile diseases has never been subjected to a thorough study. The discovery was made by Redtenbacher that at the height of genuine pneumonia the chlorides disappear completely or almost completely from the secretion of the kidneys. Hardly any studies exist which confirm this observation and provide information about the behavior of chlorine elimination in other febrile diseases. Still less have studies of the causes of diminished chlorine (and sodium) elimination in fever been published. The problem ~~is therefore set of~~ checking once more on the fact of diminished chlorine elimination, in various febrile diseases, and ~~then proceeding~~ to investigate the causes of such diminished elimination. Determination of the quantities of chlorides taken with the food, together with voluntary augmentation of these intakes, ~~and then study of~~ the quantities eliminated through the kidneys and the intestine, ~~with due regard to any~~ elimination setting in subsequently, may well be the way by which the problem set is to be solved."

The significance that the question of chlorine elimination in fever has is best discerned when we consider it in connection with the other processes of metabolism.

We judge the metabolism of any organism, not excepting an organism in a state of fever, by observing the substances

which are eliminated as its end products through the excreta. This means for nitrogenous substances in general the urea, for non-nitrogenous ones the carbonic acid exhaled in by far the largest part through the lungs; apart from these the ash constituents must be considered, which we measure as to their varying amount in the urine and the faeces and attempt to bring into relationship with the other phenomena.

As is well known, Traube and Jochmann have already established the fact that in fever the elimination of urea is considerably increased. This shows that in fever the tissues of the body, which consist in the main of nitrogenous substances, are subject to an abnormal disintegration; for it is clear that if a greater amount of nitrogen is eliminated from the body than is ingested with the food, then the excess nitrogen can only come from the tissues of the organism itself. Whether the elevated body temperature, which according to recent investigations effects _per se_ a destruction of tissue, is the cause of this, or whether the cause is perhaps to be sought in the deleterious influence that an agent circulating in the blood exerts directly upon the vitality of the organs, is for the moment a matter of indifference to us.

As to the carbonic acid, we know chiefly from the latest work of Leyden and A. Fränkel that it shows a considerable increase in fever — a fact that is of significance especially because it shows that the higher body temperature is to be attributed, if not exclusively, at least in large part to increased oxidation.

To the firmly established facts also belongs the behavior of those ash constituents which we assume to serve in combination with the proteins to make up the tissues, for according to Salkowsky's investigations [see note], the elimination of potassium salts as well as that of phosphoric and sulphuric acids shows a considerable increase in fever. This can be readily related to the disintegration of the tissues, for since, as we have just seen, the nitrogenous substances fall prey to disintegration in fever, the ash constituents previously in combination with them must be liberated, and they then get into the circulatory system and are eliminated as substances unusable in the body's economy.

[Note] E. Salkowsky, "Studies of the Elimination of the Alkali Salts," _Virchow's Archiv_, Vol 53.

On the other hand our knowledge of the behavior exhibited by the ash constituents of the plasmatic fluids, especially chloride and sodium, during fever is still relatively slight. —

Salkowsky had found simultaneously with the above-mentioned increase in the potassium salts a reduction in the quantities of soda eliminated in the urine and faeces. With respect to the be-

havior of the chlorides, too, a number of observations are available. Redtenbacher [see note a] had already made the discovery that at the height of genuine pneumonia the elimination of chlorides in the urine is very slight, and that in fact they sometimes disappear almost completely from the secretion of the kidneys. Redtenbacher had regarded this as pathognomonic for pneumonia and related it to the formation of the exudate. Other investigators after him, Jul. Vogel, Unruh, and several others, have observed the same fact in the other, especially the acute febrile diseases. But as to what this is due to there are almost no studies available. It had been assumed that it had its basic cause in the depressed appetite and the consequent decreased intake of chlorine; but the only way that a correct appraisal of the quantities of ClNa eliminated was possible, -- a quantitative determination of the chlorine in the nourishment taken and a comparison on that basis of the quantities of chlorine ingested with the quantities eliminated, -- had not been taken. On the other hand the decrease in chlorine intake alone could not possibly explain the almost complete disappearance of chlorides not infrequently observed. Still other causes must come into play here. There were two possibilities. First, the chlorides taken in with the nourishment were not completely resorbed from the intestine; Traube had expressed this view [see note b]. Second, the chlorides taken in were completely resorbed, but were not eliminated in their total amount from the kidneys, so that their retention in the body was taking place. This again could have a double cause.

[Notes] a) Zeitschrift der K.K. Gesellschaft der Aerzte zu Wien (Journal of the Imperial and Royal Society of Physicians at Vienna), August 1850.

b) L. Traube, Die Symptome der Krankheiten des Respirations- und Circulationsapparates (The Symptoms of the Diseases of the Respiratory and Circulatory System), Berlin, 1867, page 114.

First, it could be due to a deficient capability of the kidneys to function. The depression that the activity of many other glands shows in fever pointed in that direction. The secretion of saliva stops (hence the dryness of the mucous membrane of the mouth and throat), and in particular the sweat glands, which in other respects too are regarded with the kidneys as equivalent and vicarious organs, do not function, at least in a number of febrile diseases. An alteration of the kidneys themselves is also indicated, lastly, by the decrease in elimination of water and the not infrequent occurrence of albumin in cases of intense fever.

But then it is conceivable that besides deficient capability of the kidneys to function still other causes for retention might come into consideration, which might stand in direct relation to the general metabolic processes in fever.

In view of these considerations I decided to subject the question of chlorine elimination in fever to a new treatment.

The course of the investigation lay clear before me.

In the first place I must test the food that I was going to give the patients for chlorine content by precise quantitative analyses.

I had to determine the total amount of chlorine in the excreta, and not only in the urine but also in the faeces; for if a diminution of chlorine elimination through the urine could be established, the chlorine content of the faeces must show whether deficient resorption from the intestine was to blame. That would have been the case if the chlorine in the faeces had shown an increase corresponding to the decrease in the urine. If on the other hand the chlorine content of the faeces remained unchanged, or in other words all the chlorine ingested in the food was taken up from the intestine into the organism, then an abnormally large quantity of common salt that I administered besides the food could determine whether a deficient capability of the kidneys to function might not be the sole cause of the retention. For this deficiency must appear more clearly the more ClNa was to be eliminated. If on the other hand all the common salt administered was eliminated through the kidneys, i.e. if at least as far as chlorine was concerned no impairment of kidney function was present, then I should still have to seek in other experimental ways for the cause of the diminished chlorine elimination in fever.

I shall first set down the method of the investigation, then the experiments themselves and their results.

Method of the Investigation

The patients I made my studies on were given to eat: milk, coffee, and rolls (typhus patients only milk and coffee); then, when the appetite became heartier, raw beef and raw eggs were added. To drink they were given sol. gumm. citrica in any amount desired. -- At the maximum the patients received 310 ccm of coffee, 1800 ccm of milk, two 76-gram rolls; or no coffee, 2350 ccm of milk, and three rolls. In addition to that in some cases 330 g of beef and 1-3 eggs.

The milk and the coffee were measured out by a reliable waiter with vessels whose average content I had previously determined.

The computation of the chlorine content of the beef and the rolls was based on the average weight.

Analyses of the Food
I. Determination of the ClNa

1. Milk. — Bunge's analyses [see note] of milk were available. He had found in cow's milk 1.19 to 1.709 per mill Cl (= 1.96 to 2.81 ClNa). But since it was to be assumed from the outset that Berlin milk, and especially the milk at the Charité, did not have the same composition as the unadulterated milk of the Dorpat cows, I ran three analyses by Bunge's method of the milk that was given to the patients. I found in

1000 ccm of milk 1) 1.56 g ClNa
2) 1.55 " "
3) 1.54 " "

[Note] Der Kali-, Natron-, Chlorgehalt der Milch (The Potassium, Soda, and Chlorine Content of Milk), inaugural dissertation, Dorpat, 1874.

2. Coffee. — 100 ccm of the beverage offered as "coffee," i.e. milk with coffee, was incinerated in the same manner as milk with the addition of carbonate of soda and contained on the average of two analyses of high correlation 0.0175 g ClNa.

3. Rolls. — In determining the chlorine content of the rolls I proceeded as follows: about 150 g of moist substance was cut in small pieces, weighed to an accuracy of one centigram, and dried on the water bath in a flat dish. After cooling it was again weighed and pulverized in a mortar. Of the powder I took 20 to 25 g (to the nearest centigram), mixed it with 1 to 2 g of finely powdered sodium carbonate, and carbonized it in a large open platinum crucible over the lowest possible flame.

The coal was extracted repeatedly with water and then incinerated, the ash after cooling dissolved with cold dilute nitric acid, and combined with the extract. The still alkaline liquid thus obtained was treated with dilute nitric acid drop by drop to the point of weak acid reaction and the chlorine determined by titration with $AgNO_2$.

100 g of moist roll contained 1.304 g ClNa
1.322 g "
1.360 g "

4. Beef. — 1000 g contains 1.135 g ClNa according to Voit (Untersuchungen über den Einfluss des Kochsalzes etc. (Studies of the Influence of Common Salt, etc.), Munich, 1860, page 42.).

5. Eggs. — Statements concerning the chlorine content of eggs differ quite considerably, but it is so slight that I believed I was justified in ignoring it.

Data:

1000 parts albumen contain 6.60 inorganic salt (Lehmann) [s. note]
100 " ash,
albumen 41.29, 42.17 ClK } Poleck
9.16, 14.07 ClNa }
39.30 ClNa according to Weber.
yolk: no Cl according to Poleck,
9.12 ClNa " " Weber.

[Note] Cf. Gorup-Besanes, Phys. Chemie (Phys. Chemistry), 1875, page 746.

The ash of eggwhite and yolk of two infertile eggs, each egg set = 100, contains according to Lehmann [see note]:

eggwhite	0.994	0.093
eggyolk	0.039	0.028
	0.133	0.121

[Note] Zoochemie (Zoochemistry), 1858, page 287.

1) 100 ccm of milk contains 0.46 g of N [see note a]. This corresponds to the nitrogen of 0.985 g of urea.
2) 1 roll contains 0.95 g N [see note a] = 2.036 g urea.
3) Eggyolk. 100 g moist = 2.606 g N [see note a]
15.04 g [see note b] = 0.404 g N = 0.860 g urea.
4) Eggwhite. 100 g = 1.93 g N [see note c].
23.01 g [see note b] = 0.096 g N = 0.207 g urea.
5) Beef. 100 g = 3.4 g N [see note d] = 7.286 g urea.

[Notes] a) A. Fränkel, Charité-Annalen (Annals of the Charité), Vol II, page 326, note.
b) Lehmann, Zoochemie, 1858, page 285.
c) Voit, Zeitschrift für Biologie (Journal of Biology), Vol II, 1866.
d) Voit, Zeitschrift für Biologie, Vol I, pages 97 ff.

The food, whose chlorine and nitrogen content I thus knew completely, was given to the patients daily at the same time.

The last urine was passed by the same patient always at the same hour, -- by some at 10 p.m., by others at 11 p.m., and by still others at 12 p.m. -- The date shown refers to the day preceding the last discharge. In the same way the faeces were designated by the date of the same day indicated for the corresponding 24-hour period for urine.

In the urine the chlorine was determined by combustion with saltpeter and titration with silver nitrate [see note], and the urea by Liebig's titration method.

[Note] Cf. Neubauer and Vogel, Analyse des Harnes (Analysis of the Urine), 1872, page 168.

The faeces were discharged into a clean bedpan, taken from it with a spoon, and put into a weighed porcelain dish. Small losses were unavoidable in this process, but in considera-

tion of the low common salt content of the faeces these losses played no part.

In order to obtain as uniform a mass as possible, the faeces after being weighed were triturated in a mortar. Of this a sample of 10 to 20 g was taken and accurately weighed in a suitable platinum dish with a cover to the nearest milligram. If I was not able to work up the faeces immediately, since I sometimes had chlorine determinations to make for two patients at the same time, the weighed and triturated faeces were evaporated either wholly or in a rather large sample on the water bath until dry, the air-dried mass again weighed after cooling and then pulverized and kept in a system of watchglasses.

Of this powder a sample weighed to the nearest milligram was later used for analysis.

The analysis was carried out as follows: The weighed sample in the platinum crucible was stirred up with about 2 ccm of a saturated solution of carbonate of soda and evaporated to dryness; it was then carbonized over the least possible flame and the cooled coal repeatedly extracted thoroughly with hot water and filtered; the filter with the extracted coal was dried on the water bath and incinerated at a faint red heat, the crucible being incompletely covered. The ash was again extracted and filtered and the filtrate combined with the first extract. The ash was then heated to a strong red glow until as much as possible of the coal was burned up. From that point on the procedure was the same as described above for the roll.

In extracting the coals of milk, rolls, and faeces I always first obtained a black liquid unusable for titration. In this case I brought the incineration to an end in the usual way. Then I evaporated the entire quantity of liquid to dryness and incinerated it again at quite low temperature. Later I decolorized the black liquid with calcium carbonate, filtered off the pricipitate, washed out the filter thoroughly, and concentrated the now clear, definitely alkaline liquid on the water bath, then added dilute nitric acid to the point of weak acid reaction, neutralized the acid with calcium carbonate, and determined the Cl as ClNa by titration with silver solution. — But after I had acquired a certain amount of practice I saw that this complicated procedure could be avoided if I carbonized the substance in question carefully but thoroughly in the first place.

Experiments and Results
A. Chlorine Elimination under Normal Conditions

According to Voit's investigations, under normal conditions the entire amount of common salt taken in with the food is eliminated through the kidneys. Differences between intake

and elimination occur only when one changes from a high-chlorine to a low-chlorine diet or conversely from a low-chlorine to a high-chlorine diet, and then in the former case more and in the latter case less common salt is eliminated until equilibrium is achieved between the quantity of chlorine taken in and the quantity eliminated. -- According to this if an organism in a state of chlorine equilibrium is suddenly given a large quantity of common salt in addition to the previous diet, then this additional quantity leaves the body completely in a short time and the former equilibrium is soon reestablished.

The quantity of water, as Voit also demonstrated, plays a considerable part in the elimination of chlorine.

In the following experiment performed on myself is shown the behavior just described of a normal organism in a state of chlorine equilibrium upon the introduction of a fairly large quantity of common salt, and also the low chlorine content of the faeces and incidentally the increase in discharge of urine under the influence of common salt.

The daily food intake throughout the duration of the experiment was: 2 cups of milk, 2 French rolls, 300 g bread, 50 g unsalted lard, 450 g beef, 1/2 liter of beer, about 1 liter of water, 5 g common salt. -- The beef was fat-free and was freed of sinews in a meat-cutting machine before weighing. The preparation consisted in its being fried in my presence with a part of the weighed lard.

Date 1878	Urine			Faeces		Urea
	Volume	Spec. Gravity	ClNa	Weight	ClNa	
3 Jan.	1275	1020	10.582	147.8	0.045	
4 Jan.	1375	1018	8.937	82.7	0.027	41.25
5 Jan.	1480	1018	8.880	203 thin, pulpy	0.162	43.51
6 Jan.	1305	1019	8.220	87.3	0.041	43.48
7 Jan.*	1395	1022.5	12,415	208.2 some diarrh.	0.154	52.17
8 Jan.	1325	1020	9,407	--	--	--
9 Jan.	1430	1019.5	10.158	67.35	traces	
10 Jan.	1270	1019.5	7.239	--	--	45.46

*On 7 January intake of 5.39 g of calcined ClNa. The irregularity in discharge of urine on 9 and 10 January is the result of my having been unavoidably kept from going to bed on the former day until 2 in the morning. The average of 10.15 and 7.2 is 8.6, or almost exactly the average of the chlorine figures for the three days before taking the common salt.

B. Chlorine Elimination in Acute Febrile Diseases

Of all the acute febrile diseases that I had the opportunity to observe during the 1877-78 winter half-year, unfortunately only the three cases of pneumonia described below were suited to complete investigation. Nevertheless, the results obtained in these cases can be transferred without misgivings to the other acute illnesses, which terminated critically, since on the one hand many authors, e.g. Unruh for relapsing fever and typhus exanthematicus, have found a similar and in some cases even a much more significant dwindling of the amount of chlorine [see note], and on the other hand there is no reason for assuming that the cause of diminution of the chlorine in the urine in those diseases is different from the cause in pneumonia.

[Note] W. Brattler, Ein Beitrag zur Biologie (A Contribution to Biology), Munich, 1858. -- Moos, Henle und Pfeufer's Zeitschrift (Henle and Pfeufer's Journal), new series, Vol VII, No 3. -- Unruh, Virchow's Archiv, Vol 48.

Let us now proceed to consideration of the individual cases, beginning with the Weiss case.

A glance at the column in the accompanying table which shows the difference between the amount of chlorine [see note] ingested and the total amount eliminated in urine and faeces shows at the height of the fever a definite retention of common salt; this does not seem very considerable on the first day of observation, under the influence of the food taken previously, but on the second day it amounts to 2 grams. With the onset of crisis this retention ceases, changing over into an epicritical Cl elimination of about 4.3 g. Unfortunately a day is missing at this point. The ClNa elimination declines until equilibrium between intake and elimination is reached, but then rises again during convalescence; about 14 days after the crisis the elimination in the urine comes to the enormous amount of 34 g ClNa.

[Note] In the tables the chlorine is computed in terms of ClNa, and for that reason I sometimes use chlorine and ClNa interchangeably in the text as well.

A much more considerable retention appears in the Lange case. After the influence of previous nourishment ceases on the second day, a retention of chlorides begins. This lasts until the fourth day after the return of normal temperature. At that time more than $7\frac{1}{2}$ g is left in the body, and not until the fifth day does an over-elimination of 3 g occur [see note].

[Note] Similar cases of late-starting postfebrile ClNa elimination are found in Unruh, loc.cit.

Lastly, we also see a retention in the Puder case, which is especially characteristic in the postfebrile elimination

of ClNa, totaling 11½ grams. In the beginning of convalescence we again find at first a diminution of the elimination, but we are unable to say whether this is a consequence of the new formation of body tissue or whether it too will be followed in the next few days by a correspondingly increased elimination.

In the Weiss and Lange cases the chlorides of the faeces were measured. The figures in the appropriate column show that in the case of Weiss (perhaps chiefly as a result of diarrhea) the chlorides are somewhat increased, but in the case of Lange they are practically the same as the norm. In other words, the chlorides ingested in the food are as good as completely taken up from the intestine; a deficient resorption is not the cause of the disappearance of ClNa from the urine, but instead there is a retention of it in the body.

Of other acute febrile diseases I adduce only incidentally the Massfeller case (typhus exanthem.) and the Kummer case (measles). In the former case the investigation had to be broken off at only the third day because of too great stupefaction of the sensorium. On the first day we see a trifling retention of about 0.4 grams, on the second an over-elimination of only 0.1 g, or in other words a tendency to retention.

The Kummer case is interesting because of the great epicritic ClNa elimination and the slight chlorine content of the faeces. I am not giving figures for the common salt intake because I was not furnished with absolutely accurate information about the quantity of food taken. (This was the first case that I studied in this way.)

C. Chlorine Elimination in Subacute Febrile Diseases

The following two cases of inflammatory rheumatism (Douceur) and ileotyphus (Korkhaus) are intended primarily to serve to demonstrate the behavior of chlorine elimination in subacute febrile diseases. At the same time an attempt was made to decide by the administration of abnormally large quantities of common salt the question of whether the retention found above in the acute febrile diseases is due to a deficient capability of the kidney to function.

In the Douceur case during the first few days there is an over-elimination of ClNa, which is due as under normal circumstances to the influence of the previous food of higher salt content. The over-elimination of about 8 g on the third day of observation has its cause in the fact that the patient admittedly ate cake and other things on a visiting day in addition to the diet. — On the 4th, 5th, and 6th days there is a retention of ClNa, which as far as the 6th day is concerned can be attributed mostly to the relatively small amount of urine. On the following day an over-elimination corresponding to the retention takes place and the 10 g previously retained leaves the body

completely, in spite of a high temperature, under the influence of a larger amount of urine. From here on we see retention alternate with over-elimination, in such a way that each time the amount retained corresponds to an almost absolutely equal over-elimination. This is all the more interesting in view of the fact that on the ninth day of illness 4.65, on the eleventh 6.3, and on the twelfth 2 grams of common salt was administered directly as such.

Conditions are similar in ileotyphus (Korkhaus). Appraisal of the elimination on the first days is complicated here by the fact that at the same time that the influence of the previous higher-chlorine diet still continues, 4.65 g of ClNa was administered. Nevertheless, in spite of the artificially increased intake, there is no retention. On the fourteenth day of illness the difference between the ingested and eliminated quantities of chlorine is equal to zero. On the fifteenth day of illness the patient was again given 5 g of common salt in addition to his food; of this amount 2 1/2 grams was retained, but on the following day not only this 2 1/2 grams but about 4 grams more was eliminated. This last is accounted for in my opinion by the extraordinarily increased elimination of water (over 5 liters in one day). After an equilibrium has been reached between intake and elimination, with the return of normal temperature, there is in convalescence a slight over-elimination, analogous to the epicritical chlorine elimination in acute febrile diseases.

In the two subacute febrile diseases available for study, then, no retention of the chlorides taken in with the food has been proved. This is not to say that diminution of chlorine elimination and retention do not occur in these diseases, too, particularly in ileotyphus; on the contrary, the information already cited from Moos, Brattler, and Unruh decidedly indicates their occurrence.

Secondly these two cases show us that chlorides, even when introduced in abnormally large amounts, in spite of significantly heightened body temperature are eliminated completely and in the same way as under normal conditions, by the kidneys [see note].

[Note] The objection that I tested the capability of the kidneys to function with respect to chlorine elimination only in cases where I obtained no retention at all I intend to check by further investigations.

<u>Conclusions</u>

On the basis of the above experiments we arrive at the following results:

In the acute febrile diseases a greater or lesser part of the chlorides taken in in the food is <u>not</u> eliminated through the kidneys.

This retention is not due to a deficient resorption from the intestine, for the chlorine content of the faeces is very low. Neither is it due to any inability of the organism to eliminate the quantities of ClNa ingested; this is denied by the abnormally large quantities of common salt arbitrarily introduced during fever and completely eliminated by the kidneys.

It thus only remains to consider the possibility that the general metabolic processes in fever are the essential cause of the retention.

We have already pointed out above that the salts in the body [see note] exhibit a different behavior depending on whether they serve like the salts of potassium and phosphorous in combination with the organ albumin to constitute the tissues or whether they circulate in the plasmatic fluids. Just as the organ albumin itself falls prey only to a very slight degree to the disintegration processes, so the salts combined with it undergo only a slight change. In the plasma, on the other hand, the quantity of salts changes every moment; it is dependent on the ash constituents taken in in the food and on the conditions which effect their elimination from the body. But among them, too, two groups must be distinguished. One group -- the so-called free salts -- are in simple solution or are bound to the end products of regressive metamorphosis. These can always be eliminated through the kidneys in amounts corresponding to the quantity in which they are present in the blood. But apart from them there is also a certain quantity especially, as concerns chlorine, of sodium chloride that is bound to the circulating albumin and can no more be eliminated by the kidneys than the albumin itself.

[Note] Cf. Dr. J. Forster, "Experiments Concerning the Significance of the Ash Constituents in the Diet," Zeitschrift für Biologie, Vol IX, 1873.

This relationship of the sodium chloride to the circulating albumin is of the greatest importance in our present question, inasmuch as it offers us the possibility of explaining why the chlorides show such a striking diminution in the urine in fever. Let us suppose that there is a certain amount of sodium chloride in the plasma of an organism and a corresponding amount is eliminated in the urine, and let us then suppose that a certain quantity of albumin gets into the plasma. What will the consequence be? The albumin will enter into combination with a corresponding part of the free sodium chloride present, it holds this back in the body, and not the same amount of sodium chloride will be eliminated through the urine as before, but as much less as the amount of sodium chloride that has entered into combination with the albumin substances.

We have a quite similar process in fever. Here more or less of the tissue disintegrates, and organ albumin becomes

circulating albumin. Only a part of this is immediately decomposed into its end products; the rest, as the behavior of nitrogen elimination during and after fever shows, is retained in the body. In the plasma it combines with the sodium chloride, prevents it from being eliminated, and thus brings about the diminution of chlorides in the urine. When during and after the crisis the retained quantities of albumin break down and their nitrogen is removed from the body with the critical and epicritical urea elimination, then -- and only then -- the sodium chloride becomes free and leaves the organism in an amount corresponding to the earlier retention.

The reason for the fact that especially in acute febrile diseases a certain part of the chlorides taken in in the food does not reappear in the urine is thus not a deficient resorption from the intestine, not a disturbance of the functioning of the kidney, but the relationship of the circulating albumin to the sodium chloride in the plasma. From this point of view it is also easy to explain why in subacute febrile diseases we sometimes (as in the cases under consideration here) find no retention. For in longer-lasting fever a point must come when the plasma has reached the maximum of its receptivity for albumins, or in other words when no more sodium chloride is needed for combination with them; retention then ceases, and just as much sodium chloride is eliminated through the kidneys as is taken in in the food.

Moreover the cases e.g. of ileotyphus (cf. Brattler, Moos, Unruh, loc.cit.) would agree with this in which in the first few days -- that is at a time when the maximum for absorption of albumin had not yet been reached -- the amount of chlorine in the urine sank to a minimum, but then gradually rose again (until chlorine equilibrium came about).

The view that albumin particles combine in the plasma with a part of the free sodium chloride is supported by Forster's experiments in which he found that when the ash constituents are cut out of the diet and abundant albuminates are fed, less salts appear in the urine the more albuminates have been taken in. In conformity with this Forster also found that even after long chlorine hunger the blood is still relatively rich in sodium chloride itself.

In order to demonstrate directly the influence that an increased supply of albumin has on the elimination of chlorine, I set up the following experiment.

I fed a large, powerful female draft dog for a rather long time with 100 g of air-dried, pulverized ship's biscuits, 100 g of unsalted lard, 70 g of condensed milk, 500 g of water, and 2 g of ClNa. After the dog had gotten into chlorine and nitrogen equilibrium on this diet, it was also given 750 g a day

of raw horse meat. The amount of meat was set no larger just in order not to change the conditions of elimination too much by the water content of the meat and in order to avoid the dog's rejecting the bread and milk diet.

Experiment on the Dog

[Note] For the first few days the dog had been given 150 g of bread, but on the fifth day of the experiment she vomited the whole meal. I therefore reduced the amount of bread to 100 g.

Chlorine determinations by incineration and titration did not succeed, as in spite of all efforts I never succeeded in getting a precise end reaction. I therefore determined the amount of chlorine in the ash by precipitation with $AgNO_3$, and am reporting only the results obtained by this latter method.

The weight of the dog on the first day of the experiment was 32,784 grams.

Date	Day of Experiment	Body Weight in Grams	Urine Volume	Spec.G.	Urea	Phosph.S.	ClNa	Remarks
Nov.								
10	8	30955	470	1019	12.60			
11	9	30795	500	1018	12.40	1.130	2.750	
12	10	30475	510	1018	11.93	—	2.985	
13	11	30405	360	1022	12.52	1.130	1.962	
14	12	30825	595	1033	36.65	2.618	3.570	750 g horse-meat
15	13	31145	585	1034	36.85	2.658	2.264	
16	14	31443	605	1037	42.83	2.856	2.299	
17	15	31405	625	1040	46.75	2.837	2.742	

From the amount of sodium chloride on the days when the dog was given 750 g of meat we must subtract 0.851 g of ClNa, i.e. the amount that corresponds to the chlorine content of the meat. The sodium chloride table then reads as follows:

Date	Amount of Urine	ClNa	Remarks
Nov.			
10	470	—	
11	500	2.750	
12	510	2.985	
13	360	1.962	
14	595	2.729	750 g of meat
15	585	1.413	
16	605	1.448	
17	625	1.891	

But even this table is not yet quite right for judging the behavior of the ClNa elimination; for on 13 November the amount of urine suddenly dropped, without any recognizable cause. The chlorine elimination is correspondingly less on that day, and increased again the next. If we add the amount of chlorine for these two days and subtract from the sum the average for the two preceding days, which corresponds to the chlorine equilibrium, we obtain the following figures:

Date	Amount of Urine	ClNa	Remarks
Nov.			
10	470	—	
11	500	2.750	
12	510	2.985	
13	360	2.868	
14	595	1.813	750 g of meat daily
15	585	1.413	
16	605	1.448	
17	625	1.891	

Although I admit that this experiment, in view of the irregularity just discussed, cannot be called an elegant one, still it does show, as I believe, a diminution in elimination of chlorine which is conditioned by the intake of nourishment rich in albumins. I reserve for myself an early repetition of this experiment.

In conclusion, as concerns Redtenbacher's view that the disappearance of chlorides from the urine in pneumonia (cf. Traube, loc.cit.) is a consequence of the formation of the exudate, it shows up quite clearly from the foregoing discussion that even in pneumonia this cannot be the sole or even essential cause. Whether a part of the retained chlorides is used in the formation of the exudate is a question for which no exact proof is available yet, but which could perhaps be decided by a comparison of the chlorine content of a normal and a hepatized lung.

As I bring this article to a close it is a pleasant obligation for me to express my most heartfelt gratitude to my revered teacher, Privy Councilor Prof. Dr. Leyden, and to Dr. A. Fränkel for the generosity with which the means for these investigations were put at my disposal in the laboratory and the clinic, as well as for the guidance and encouragement that I have been privileged to enjoy during this work.

Cases

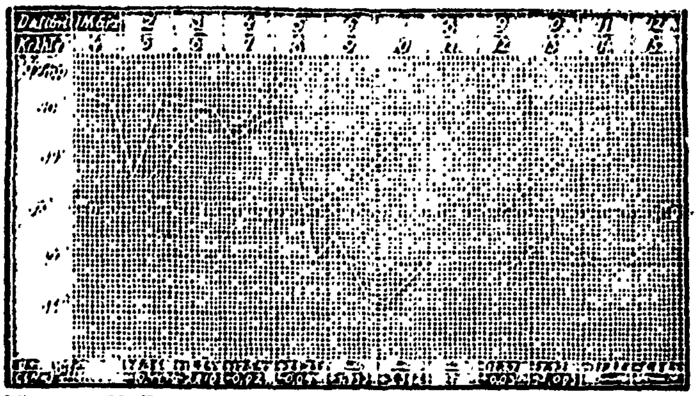
Explanation of the Graphs on the Following Pages

______ Temperature
...... Abscissa, showing the chlorine and urea equilibrium
– – – Curve of the ClNa differences
–·–·– Curve of the urea differences

The last two curves were obtained by plotting above the abscissa, i.e. as positive, the coordinates for amounts of urea and/or ClNa which correspond to over-elimination from the body, and below the abscissa those for quantities of urea and ClNa retained in the body. One millimeter of length of the coordinate always corresponds to a certain number of fractions of a gram.

The urea and ClNa differences are given again below the graphs for easier orientation.

I. Weiss, pneumonia.

a
b


a) Date (1 March, etc.). b) Day of illness.
- - - Curve of ClNa differences: 5 mm coordinate length = 1 g of ClNa.
-·-·- Curve of urea differences: 1 mm coordinate length = 1 g of urea.

Day of March 1878	Day of Illness	Temperature a.m.	Temperature p.m.	Urine: Volume	Urine: Specific Gravity	Urine: ClNa	Faeces: Weight	Faeces: ClNa	ClNa: Eliminated in Urine & Faeces	ClNa: Taken in in Food	ClNa: Intake minus Elimination	Urea: Eliminated in Urine	Urea: Computed from Nitrogen Content of Food	Urea: Difference
1	4	40.3	40.1	—	—	—	13.7	0.670						
							air-dried							
2	5	38.6	40.2	870	1014	3.480	166	0.242	3.722	4.166	-0.444+x	22.44	17.08	+ 5.36
										bouillon				
3	6	40.1	40.0	1360	1014	2.720	284	0.243	2.963	4.973	-2.010	40.55	22.29	+18.24
4	7	39.4	39.8	1390	1012	2.910	596	0.060	2.970	2.966	+0.016	35.76	18.22	+17.54
5	8	39.9	37.0	3250	1006	2.925	—	—	2.925	2.966	-0.041	47.45	18.22	+29.23
6	9	37.5	36.3	2710	1008	3.937	273	0.122	4.059	2.966	+1.093	—	18.22	—
7	10	36.2		1840	1015	5.980	518	0.348	6.328	2.966	+3.362	—	18.22	—
		normal												
8	11	"		thrown away			350	0.370	?	5.446	?	?	42.04	—
9	12	"		1920	1011	5.184	607	0.717	5.477	5.446	+0.031	29.77	42.04	-12.27
10	13	"		2335	1009	7.092			7.451	5.446	+2.005	34.12	42.04	- 7.92
11	14	"		1940	1012	8.596	259	0.215	9.333	convalescent		28.13	40.01	-11.88
12	15	"		1745	1012	9.074	—	—	9.074	diet		33.39	40.01	- 6.62
23				3725	1011½	3.445								

Urine at first contained some proteins. Faeces diarrheic; 6 March pulpy, 7 March diarrheic, from then on thin-pulpy. — x denotes the amount of ClNa taken in bouillon on that day only.

The patient, a 43-year-old big, strong workman, fell ill on 26 February with with a hard chill. Coughing set in at the same time, but with little or no expectoration, no pain in the chest. On the right side below the scapula, somewhat re-

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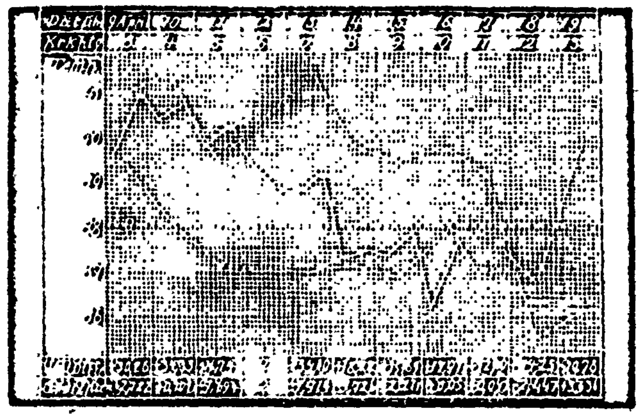
duced resonance; in that region bronchial expiration and crepitant râle. Coughing fairly slight. Sputum amounts to about 2 tablespoons and is largely fluid, foamy, only a little glassy, of a grayish yellow appearance; only once did it appear definitely rust-colored. Treatment: cold baths.

II. Lange, pneumonia.



a) Date. b) Day of illness.

- - - Curve of ClNa differences: 5 mm coordinate length = 1 g of ClNa.

-·-·- Curve of urea differences: 1 mm coordinate length = 1 g of urea.

Day of April 1878	Day of Illness	Temperature a.m.	Temperature p.m.	Urine: Volume	Urine: Specific Gravity	Urine: ClNa	Faeces: Weight	Faeces: ClNa	ClNa: Taken in in Food	ClNa: Eliminated in Urine and Faeces	ClNa: Difference	Urea: Computed from Nitrogen of Food	Urea: Eliminated in Urine	Urea: Difference
9	3	39.6	41.0	1200	1015	7.471	225	0.447	4.973	7.695	-2.722	22.29	53.55	+30.26
10	4	40.4	40.9	1270	1016	4.064			4.166	4.267	-0.101	17.08	51.41	+34.33
11	5	39.8	40.3	1075	1018½	2.472	—	—	4.166	2.427	-1.694	17.08	33.82	+16.74
12	6	39.5	38.9	thrown		away	—	—	—	—	—	—	—	—
13	7	38.7	39.2	980	1020	2.254	—	—	3.004	2.252	-1.914	14.73	48.72	+34.00
14	8	37.3	37.5	930	1021	2.418	82	0.022	4.973	2.440	-1.726	22.29	40.51	+18.22
15	9	37.4	37.9	970	1010	2.716	172	0.046	4.973	2.762	-2.211	22.29	37.98	+15.69
16	10	36.2	37.7	1260	1019	4.914	124	0.109	4.973	5.023	-0.050	22.29	40.19	+17.91
17	11	normal		1015	1019	4.466	—	—	4.973	4.466	-0.407	22.29	34.39	+12.10
18	12	"		1475	1013	5.605	140	0.133	8.153	5.708	-2.447	46.70	32.45	+14.25
19	13	"		1310	1017	9.039	—	—	5.353 + x salt	9.039	-3.636	46.70	36.02	+10.78

Consistency of the faeces: On the first day thin-pulpy, afterwards pulpy. — Of the first day's volume of urine about 200 ccm is missing. On the 7th and 8th days of illness moderate sweating. - x denotes the amount of salt taken with the beef and unfortunately not measured.

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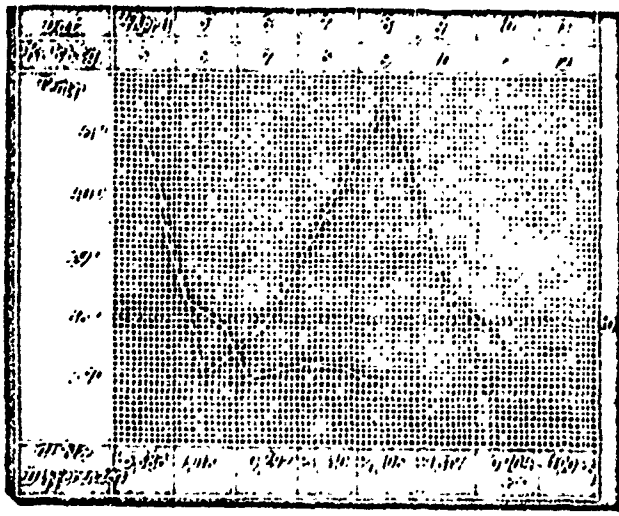
The patient, a 42-year-old moderately powerful workman of medium stature, fell ill in the night of 6-7 April, with a hard chill, slight coughing, pains in the left side. -- Expectoration about 3 tablespoonfuls, tough, glassy, definitely rusty brown in color. Lower left back, marked loss of resonance to the middle of the scapula, bronchial breathing, bubbling râle.

III. Puder, pneumonia.



- - - Curve of the ClNa differences: 5 mm coordinate length = 1 g ClNa.

Date April 1878	Day of Illness	Temperature a.m.	Temperature p.m.	Urine Volume	Urine Spec.Gravity	Urine ClNa	ClNa in the Food	Difference
4	5		39.7	1920	1017.5	9.645	3.762	-5.883
5	6	38.3	37.9	1340	1019	4.958	5.976	-1.018
6	7	37.0	37.2	1015	1023	5.684	5.976	-0.292
7	8	37.3	37.2	970	1027	8.283	4.973	-3.310
8	9	normal		1015	1025	12.078	4.973	-7.105
9	10	"		850	1021	6.290	4.973	-1.317
10	11	"		810	1023.5	4.649	5.353	-0.704- x
11	12	"		1030	1020.5	5.353	5.353	-1.000- x

x denotes the salt that the patient put on the raw beef he ate, which amounted to at least 1 to 2 grams.

The patient, a 26-year-old tall, powerful workman, fell ill on 31 March with a hard chill, coughing, sharp pain in the right side, and according to his report a reddish expectoration. In spite of his complaints he went on to work and on 4 April came to the Charité. Here a lack of resonance was found in the region of the lower right lobe of the lung, along with bronchial breathing and a slight crepitant râle. The sputum was scanty, glassy, not rust-colored.

IV. Massfeller, typhus exanthematicus.

Date March 1878	Day of Illness	Temperature a.m.	Temperature p.m.	Urine Volume	Urine Specific Gravity	Urine ClNa	ClNa Taken with Food	ClNa Elim. in Urine	ClNa Difference	Urea Taken with Food	Urea Elim. in Urine	Urea Difference
25-26	5-6		40.4[1]	760	1021.5	2.204	1.952	2.204	-0.252	13.46	46.45	-32.99
26	6	40.3[2]		255	1020	0.586	1.309	0.586	-0.723			
26-27	6-7		40.4	815	1021.5	2.608	2.159	2.608	-0.449	20.82	50.20	-29.38
27	7	40.1		305	1020	0.985	1.210	0.985	-0.265			

The temperature was taken at 6 a.m. and 6 p.m. — The urine was grouped into two periods, one lasting from 4 p.m. until 10 a.m. of the next day, the other from 10 a.m. to 4 p.m. of the same day. — [1]One bath. [2]Two baths, at 16° Réaumur, with cold affusions.

The patient, a 24-year-old mechanic of heavy-set build, had complained for 8 days of lack of appetite, a slight cough, and headache. Four days before, an exanthema of abundant reddish spots appeared on his body and lower extremities. Because of a general feeling of illness the patient came to the Charité on 25 March. — The course of the disease corresponded to that of exanthematic typhus. Because of too great stupor of the patient the examination had to be broken off. No faeces were available at the time.

V. Kummer, measles.

Date Dec. 1878	Day of Illness	Temperature a.m.	Temperature p.m.	Urine Volume	Urine Spec. Gravity	Urine ClNa	Faeces Weight	Faeces ClNa
6	5		39.4					
7	6	39.6	38.8	600	1020	3.420	674	0.878
8	7	37.8	37.1	1310	1014	2.882		
9	8	36.9	37.0	2070	1007.5	8.280		
10	9	normal		1730	1014	10.65		

The patient, a strong 19-year-old journeyman mason, fell ill during the night of 1-2 December 1877 with severe headache and hot and cold sensations. In spite of the fact that the patient felt very unwell, we went to work and did not come to the Charité until 6 December, with severe conjunctivitis, nasal catarrh, and an eruption of confluent red vesicles which spread from the face all over the rest of the body. Double catarrh of the lower parts of the lungs.

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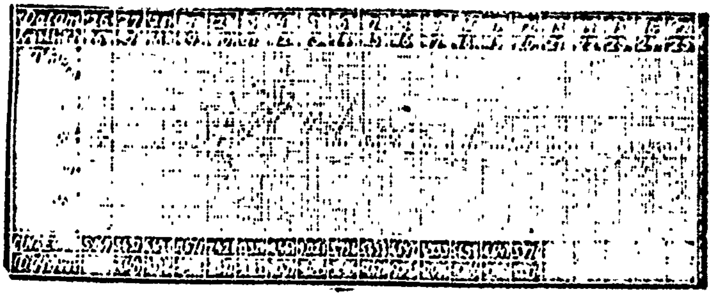
VI. Douceur, acute inflammatory rheumatism.



*The patient admittedly took in addition to the diet other food (cake) brought to him by relatives when they visited him.

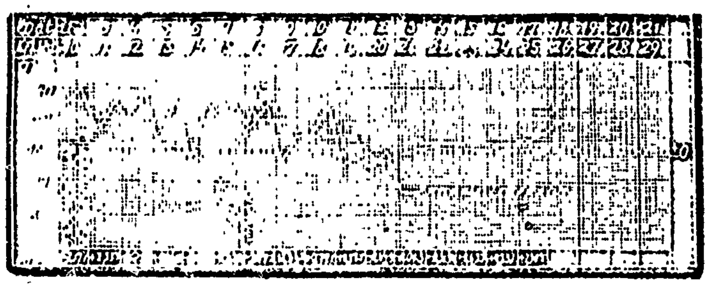
- - - Curve of the ClNa differences: 3 mm coordinate length = 1 g ClNa.

Date in 1878	Day of Illness	Temperature a.m.	Temperature p.m.	Urine: Volume	Urine: Specific Gravity	Urine: Urea	Urine: ClNa	Faeces: Weight	Faeces: ClNa	Total ClNa: Eliminated in Urine & Faeces	Total ClNa: Taken in in Food	ClNa Eliminated Minus ClNa Taken in
Feb 26	6	39.1	38.6	1440	1016	—	—				5.119	
27	7	37.6	38.9	925	1025	42.55	6.290			6.30	5.637 2 eggs	-0.664
28	8	37.7	38.5	2350	10165	56.40	15.510!	70.7 solid	0.034	15.52	6.641 "	-8.880!*
Mar 1	9	38.4	39.1	2175	1016	52.63	10.657			10.67	11.671 "	-1.003
2	10	37.6	39.4	1640	1018	45.26	7.052	115.9 solid	0.048	7.10	7.421 "	-0.321
3	11	38.2	39.0	920	1026	41.67	4.142	77 solid	0.039	4.17	13.32 "	-9.141
4	12	38.8	39.4	1415	1017	28.86	18.340	—	—	18.340	10.46 "	-7.879
5	13	38.4	39.1	1425	1024	59.28	11.115	—	—	11.115	9.02 "	-2.094
6	14	38.4	39.4	1660	1022	—	6.142	208 pulpy	?	6.14-x	5.73 "	-0.40-x
7	15	37.8	38.7	900	1026	—	3.060	218 solid prtly pulpy	0.108	3.16	5.638 1 egg	-2.470
8	16	38.2	37.8	1565	1020	50.08	8.983	—	—	8.98	6.641 "	-2.342
9	17	37.6	37.8	860	1028	—	4.644	—	—	4.644	4.733	-0.089
10	18	37.4	38.7	1850	1017	45.88	3.000	270 pulpy	0.148	3.478	5.638	-2.160
11	19	38.3	38.8	1420	1018	38.82	4.458	163 pulpy	0.092	4.550	6.641	-2.091
12	20	37.5	38.5	2030	1014	31.66	9.947	—	—	9.947	5.976	-3.971
13	21	37.5	37.8	1850	1014	32.85	4.693	—	—	4.693	4.432- soup	
14	22	37.3	36.9	2425	1012	13	13.095	not collected		mixed diet: soup, roast, etc.		
15	23	37.3	38.0	2185	1015	33.21	17.80					
16	24	37.1	38.0	800	1026	—	8.48					
17	25	37.2	38.6	1160	10205	—	15.66					

x = chlorine content of the faeces

The patient, a twenty-one-year-old, somewhat weakly workman, fell ill on 22 April with pains in the hip joints, which soon spread to the other joints and were accompanied by swelling. From 1 March on a moderate loss of resonance was observed on both sides at the back, with weak, uncertain breathing in the same region.

VII. Korkhaus, ileotyphus.



- - - Curve of the ClNa differences: 5 mm coordinate length = 1 g ClNa.

For the table for this case see the next page.

The patient is a 19-year-old, short, moderately strong journeyman baker. After a prodromal stage of about 1 1/2 weeks, during which the patient complained of general weakness, lack of appetite, nausea, etc., on 24 January he had a hard chill, went to bed, and as the condition grew worse, came on 1 February to the Charité. Definitely palpable tumor of the spleen, typhus tongue, on 2 February (tenth day of illness) roseola, at first sparse, later more abundant. Diarrhea. — Treatment: baths.

Date Feb. 1878	Day of Illness	Temperature a.m.	Temperature p.m.	Urine Volume	Urine Specific Gravity	Urine Urea	Urine ClNa	Faeces Weight	Faeces ClNa	Total Eliminated in Urine & Faeces	ClNa Taken in Food	Difference
2	10	39.5	40.1	1830	1018	—	6.039	349	?	6.039	7.210[1] - x	-1.171 + x
								diarrheic				
3	11	38.6	39.6	1940	1010	—	3.104	503.47	0.380	3.484	0.949 1 egg	+2.535
								peasoup				
4	12	39.0	39.9	partly thrown	(1003.5) away	—	0.7%	283	0.074	—	1.352	+ -
								peasoup				
5	13	38.2	39.8	2755	1003	—	2.204	285.8	0.403	2.607	2.159	+0.448
								a little	less thin			
6	14	37.7	39.6	2885	1006.5	34.32	2.308	332.3	0.204	2.512	2.563	-0.051
								somewhat	thicker			
7	15	39.0	39.5	2605	1010	33.86	4.689	—	—	4.689	2.159-5.06[2]	-2.530
8	16	38.7	39.5	3610	1005	44.76	6.498	558.5	0.237	6.735	2.563	+4.172
								diarrheic				
9	17	37.7	38.5	3517	1005	42.17	3.868	396.6	0.057	3.925	2.563	+1.362
								peasoup				
10	18	38.5	39.5	4192	1006	47.37	3.354	—	—	3.354	2.563	+0.791
11	19	37.6	37.8	5135	1004.5	48.27	3.544	—	—	3.544	2.563 1 eggyolk	+0.981
12	20	37.5	38.0	2945	1006.5	40.64	1.914	—	—	1.914	2.563 "	-0.649
13	21	36.7	36.7	3900	1006	40.12	2.550	—	—	2.550	2.563 "	-0.013
14	22	normal		3162	1007	38.26	3.004	thrown	away	c.3.004	2.563 2whole eggs	+0.441
15	23	"		3230	1007	39.73	4.119	—	—	4.119	3.566 3 "	+0.633
16	24	"		2410	1010	34.22	4.097	87.7	0.026	4.123	3.566 2 "	+0.531
								solid				
17	25	"		1660	1012.5	34.19	6.474	107	0.025	6.499	4.569 2 " and mashed potatoes	+1.905+x
								hard				
18	26	"		1842	1014	31.86	14.552	193	0.138	Mixed diet.		
19	27	"		1970	1013.5	—	14.875	hard				

Notes. — The urine contains rather a good deal of protein.
[1]4.65 g of this w administered directly as ClNa. [2]Administered as ClNa.
x denotes the unknown quantity of ClNa taken in the bouillon. The patient was given bouillon only on the first day.